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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,808	06/18/2007	Albert J. Wong	37075-0136-00-US	1219

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DRINKER BIDDLE & REATH
ATTN: INTELLECTUAL PROPERTY GROUP
ONE LOGAN SQUARE
18TH AND CHERRY STREETS
PHILADELPHIA, PA 19103-6996

EXAMINER	
WILDER, CYNTHIA B	

ART UNIT	PAPER NUMBER
1637	

MAIL DATE	DELIVERY MODE
10/13/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/567,808	WONG, ALBERT J.	
	Examiner	Art Unit	
	CYNTHIA B. WILDER	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) *41-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 February 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/20/2006 & 3/22/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Claims 1-40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected 41-44, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 7/9/2009.

Drawings

2. The drawings filed 2/8/2006 are acknowledged. However, Figure 7 is objected to because the drawing is difficult to read, perhaps due to copy machine artifacts in that the shading makes interpretation difficult. Applicant is required to submit a proposed drawing correction in reply to this Office action for the Figure 7.

Claim Objections

3. Claims 1, 21, 22, 26, 27, 28, 34, 37 and 40 are objected to because of the following informalities: The claims 1, 21, 22, 26, 27, 28, 34 and 40 are objected for the numerical designation of the method steps. The numerical designation of method steps recited in the claims makes it difficult to distinguish between the actual numbering of the claims and the method steps. It is suggested amending the claims by deleting the numerical designation of method steps and replacing them with either an alphabet (a) or Roman numeral (i) or some other designation that clearly distinguishes the steps from the numbering of the claims. Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 1-40 are indefinite and confusing in the steps (5) and steps (6) of claim 1 because it is unclear as to how one is to select for regions of single-stranded nucleic acids when no prior steps allude to the presence of any single stranded nucleic acid acids in the mixed population. Likewise it is unclear as to how the "coupling" step (which is defined in the spec (page 27) as a covalent linkage" or any of the prior steps results in determining alternative spliced RNA molecules from normally spliced counterpart RNA molecule. There appears to be a gap between the actual method steps and the final step of detecting alternative spliced RNA molecules from the normal spliced counterpart because none of the prior steps provides a clear nexus to detection of any alternative spliced sequences. Based on the claimed method steps as currently written, it appeared that the selection of regions of single stranded nucleic acids as recited in the step (5) is an optional process that may or may not be present and hence the step (6) would be an optional step as well. MPEP states "while minute details are not required in method claims, at least the basic steps must be recited in a positive, active fashion (see *ex parte Erlich*, 3 UsPQ2d1011, p.1011 (Bd. Pat, Applicant.

Int.1986). Given the ambiguity of the claims as currently a clear interpretation of Applicant's intent cannot be ascertained. Clarification is required.

(b) Claim 5 is indefinite and confusing because it cannot be determined if Applicant intends for the claim to be an independent claim or if Applicant intends for the claim to be a dependent claim. In either case, the claim is improper because it does not limit or define the instant invention.

(c) Claim 20 is indefinite and confusing because a clear interpretation of Applicant's intent cannot be ascertained. Specifically it cannot be determined the actual structure of the tag required for the instant invention. It cannot be determined if the tag is intended to be a double stranded structure with numerous binding regions or if Applicant is suggesting that the structure of the tag changes upon binding or something completely different.

Claim Interpretation

The claims are ambiguous and indefinite for the reasons discussed above giving a clear interpretation of Applicant's intent difficult. Thus, for the purpose of application of prior art, the claims are given the broadest, reasonable interpretation by the Examiner.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schweighoffer et al (US 6251590, June 2001) in view of Winkler et al (20040110191, January 2001). Regarding claim 1, Schweighoffer et al teach a method of identifying alternatively (differentially) spliced nucleic acid regions occurring between two physiological conditions, comprising cross-hybridization hybridization between RNA and cDNA populations belonging to distinct physiological states. Schweighoffer et al teach that this allow one to demonstrate in a convenient manner unpaired regions, i.e., regions present in RNA in one physiological conditions and not in RNAs from another physiological conditions. Schweighoffer teaches that such regions essentially correspond to alternative forms of splicing, typical of a given physiological state, and this forms of genetic elements or markers of particular use in the fields of therapeutics and diagnostics as set forth below (col. 2, lines 23-33). Schwieghoffer et al do not expressly teach the use of tags to assist in the detection of alternatively spliced sequences belonging to distinct physiological conditions.

Winkler et al teach a method comprising obtaining a first population of a target molecule from a biological sample and a second population of target molecule from a biological sample. Winker et al teach wherein the target may be a population of cDNA molecules and wherein the target sample may represent a physiological condition, such as cancer (see paragraph 0148-0153, 0167); attaching a first selectable tag to cDNA molecules of the first cDNA population and a second selectable tag to cDNA molecules of the second cDNA population, wherein the tags are different (paragraph 0110, 0115, and 0169); forming a mixed population of cDNA population of cDNA; performing

amplification of the mixed population of cDNA molecules and comparing the relative abundance of the target molecules in different populations (see Examples 1-5 and Figures 1-7). Winkler et al teach that the tags comprise unique sequences which allow specific detection of differentially expressed transcripts (see 0050-0060). Winkler teaches that adding nucleic acid tag sequences to nucleic acid populations promotes amplification and differentiation of one or more nucleic acid targets present in the nucleic acid populations in a single reaction vessel (0004 and 0037).

One of ordinary skill in the art at the time of the claimed invention would have been motivated to include unique selectable tags as taught by Winkler in the alternative spliced method of Schweighoffer et al for the benefit of improving means of detecting target nucleic acid species present in the cDNA populations in a single reaction vessel. One of ordinary skill in the art at the time of the claimed invention would have been further motivated to use of selectable tags for detecting differential expressed transcripts or alternatively spliced sequences in a mixed population because the use of distinguishable tags are within the scope of the ordinary artisan's capabilities since the they do not negatively alter, modified or affect the ability to detect variations within multiple nucleic acid sequences.

With regards to claim 2-9, Schweighoffer et al teach wherein the biological samples comprise normal or diseased tissue (see col. 3, condition A and Condition B). Schweighoffer teach wherein the sample may be tissue or cell comprising a physiological condition (infection, treatment with toxic agent or etc (col. 3 and col. 15). Winkler also teaches the embodiments of claims 2-8 at paragraphs 0047, 0151-0167).

With regards to claim 10, Winkler et al teach RNA population comprising polyA+ RNA for detection by tag (see 0220).

With regards to claims 11 and 12, Winkler et al teach that the cDNA population comprises double stranded cDNA (0033, 0047 and 0239).

With regards to claims 13-19, Winkler et al teach wherein the tag may comprises a labeling domain, a restriction enzyme domain, a secondary amplification domain, a secondary differentiation domain, or a sequencing primer binding domain (0060).

Conclusion

8. No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to CYNTHIA B. WILDER whose telephone number is (571)272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Cynthia B. Wilder/
Examiner, Art Unit 1637